number of exophthalmic goiter patients developing this findings at around 60 per cent. In fact the frequency with which exophthalmic goiter exists in patients showing no exophthalmos gives one the impression that the syndrome is improperly termed. What I wish to bring out especially is that true exophthalmic goiter patients often, irrespective of the degree of severity, in approximately 40 per cent of cases, never develop exophthalmos. True thyrotoxic adenoma never develop exophthalmos unless exophthalmic goiter is superimposed.

I also disagree with Washburn regarding the presence of an increased temperature in patients with exophthalmic goiter. As brought out in my paper, an increase in temperature does not occur from the hyperthyroidism unless an accompanying infection, more often a follicular tonsillitis, exists. Confusion in this respect has been due largely to the fact that patients with exophthalmic goiter have an increased metabolism reading and subjectively feel warm and perspire.

INFECTIOUS MONONUCLEOSIS

WITH REPORT OF FIVE CASES

By H. E. BUTKA *

Infectious mononucleosis is a definite disease entity. Its onset and general findings are somewhat similar to acute lymphatic leukemia. The early enlargement of the lymph nodes, the sore throat, often with the findings of streptococci on culture, the marked increase of the total white cell count, the brief duration of the high count, the inversion of the ratio of the polynuclears and the mononuclears, the gradual return to normal, with absence of gingival and subcutaneous hemorrhages and any marked anemia, serve to give us a picture that should not be confused with other more serious conditions.

DISCUSSION *by Newton Evans, Loma Linda; A. M Moody, San Francisco; Gertrude Moore, Oakland.*

DURING recent years several articles have appeared in various medical publications describing infectious mononucleosis under various names. Bloedorn and Houghton suggested the name, acute benign lymphoblastosis; that most commonly used in America during recent years, infectious mononucleosis, was suggested by Sprunt and Evans in 1920. These authors, as well as many others, believe the condition is synonymous with a disease better known by our older colleagues under the name glandular fever, originating with Pfeiffer in 1889.

It is interesting to note that the disease appears in epidemic form, somewhat similar to influenza. During a period of some twenty years the disease was extremely rare, and only in the last few years has the attention of physicians again been called to it.

There is a noticeable similarity in the blood findings of this disease and of certain types of leukemia. Consequently, several reports of patients suffering from leukemia with recovery, unfortunately have gained entrance to medical literature.

Morley and Tidy traced the history of infectious mononucleosis to 1921, and Tidy later discussed an interesting epidemic of twenty-four cases.

In a recent article Ruth Gilbert and Marion B. Coleman gave an account of an epidemic of glandular fever, covering a period from October, 1923, to May, 1924, with partial laboratory findings in over one hundred cases. However, only a few cases were satisfactorily studied.

Infectious mononucleosis is a disease entity belonging to the acute infectious and contagious diseases. Its incubation time is about twelve days. It affects children and young adults, but may affect older individuals. Many of the cases reported were medical students. The chief findings are: a generalized enlargement of the cervical glands, with a less constant and marked enlargement of the axillary, inguinal and abdominal lymph nodes, and splenic enlargement. The glands may be tender but are not painful. The fauces are reddened, are at times covered with what appears to be a membrane, and may be acutely painful. There is a preliminary period of malaise. The glandular enlargement appears about the third day and reaches a maximum in from one to three days. With the glandular enlargement there is a pyrexia, which is usually about 103, but may reach 105 for a day or two. It rarely exceeds 100 for more than a week. The prominent glands may subside in from five to fifteen days but may relapse, or if unilateral may occur on the opposite side. Suppuration is extremely rare and when it occurs is due to secondary infection. Glands may remain palpable for several weeks, occasionally for months. After the acute stage there is usually a prolonged period of depression for weeks or months, with some anemia. Recovery is finally complete with a negligible mortality. Occasionally there is a complication of hemorrhagic nephritis, usually without other signs of kidney disease. This occurs in about 6 per cent of cases.

The leucocyte count is increased in all cases during a definite but short period of the earlier part of the disease, the highest total count reported being 35,000, while the highest percentage of mononuclear cells found was 97.5 per cent.

In Longcope's series of ten cases reported in 1922 a rather comprehensive study was made. He described the following histologic characteristics of the mononuclear cells of the blood:

1. "A small mononuclear leucocyte identical with the small lymphocyte seen in the normal blood."
2. "A large mononuclear cell identical with the large mononuclear and transitional types found in normal blood."
3. "Mononuclear cells of a type not usually found in normal blood."

"It is the third type of cell that predominates and to which particular interest is attached. In the cases reported, these cells were somewhat larger in size than the small lymphocytes and contained oval, kidney-shaped, slightly lobulated or Reider-typed nuclei, staining deeply with Wright's stain. They were usually without definite nucleoli and were often concentrically placed in the cell. Sometimes the nucleus almost filled the cell, but at other times it was surrounded by a fair amount of basophilic protoplasm of ground glass appearance, which did not contain any definite granules. These cells varied somewhat in size and shape, and frequently it was difficult to differentiate them on the one hand from small lymphocytes and on the other from the large

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mononuclear cells. Occasionally mononuclear cells were observed with eccentrically placed nuclei and deeply stained basophilic protoplasm. Such cells resembled very closely the so-called stimulation form of Turck. In three cases the oxidase reaction showed mononuclear cells free from granules. Though a few of these mononuclear cells presented somewhat the appearance of myeloblasts, the absence of the oxidase reaction served to differentiate them from this cell, and it seems highly unlikely that they are derived from the myeloid tissue and much more reasonable to suppose that they arise from true lymphoid tissue."

With convalescence and a decrease in the leucocytes these abnormal cells gradually disappear from the blood.

Lymph nodes were exercised in two of Longcope's cases. The sections revealed hyperplasia of a type simulating Hodgkins disease.

To the sixty or more cases reported in the last few years with more or less complete laboratory data, I wish to add five that have come to my attention during 1923 and 1924. Not being hospital patients much desirable data is missing, sufficient, however, being present to establish a definite diagnosis.

CASE REPORTS

CASES Nos. 1 AND 2. Miss L. H. and her mother, February, 1923.

Daughter ill first for a period of about two weeks. Began with glandular swelling in the cervical region. Soreness of tonsillar and throat regions developed about two days after the glandular enlargement; no leucocyte count made; convalescence rapid.

Mrs. H., age 65, housewife. Onset about two weeks following the daughter's illness with glandular swelling, a sore throat developing two or three days later. Edema of pharynx so marked that she could scarcely swallow water. Cultures negative for diphtheria. White count made at height of illness revealed 29,000 leucocytes, but no differential slides were obtained at this time. Two days later count had dropped to below 20,000, at which time a differential count was made, revealing mononuclears amounting to approximately 45 per cent. Recovery fairly rapid, but requiring about four weeks in all, patient being confined to her bed for about two weeks.

CASE No. 3. Mr. J. W. H., age, 21, male, American, student. Onset rather gradual with symptoms of la grippe or cold. After these symptoms persisted for three or four days he began to develop enlargement of cervical, axillary, and inguinal glands. Two or three days after this swelling came on, throat became sore and swollen with lesions confined chiefly to the tonsils. Temperature varied up to 104 and 105, and patient became delirious. Jaundice developed with marked tenderness and enlargement of liver and spleen.

At this time, November 13, 1923, blood count revealed the following: white count, 48,000; polynuclear cells, 12 per cent; small lymphocytes, 15 per cent; large lymphocytes, 48 per cent; large mononuclears, 21 per cent; Reider cells, 3 per cent; eosinophiles, 1 per cent; making a total of mononuclear cells of 87 per cent.

During the course of the disease, patient had three epileptiform seizures, lasting only a few minutes each time. An eruption about November 18 which simulated measles with a slight suggestion of scarlet fever. This subsided in a few days and patient began to exfoliate. This continued on for about two weeks, much like scarlet fever, with sheets of scales coming off the hands and feet.

Convalescence rapid and blood count made six weeks after onset of the disease was normal.

CASE No. 4. Dr. D. D. C., physician caring for cases 1, 2, and 3.

Several days before taking first blood count patient felt indisposed with some soreness of throat. This became more severe and after a few days marked swelling of the lymph nodes over entire body was noted, and especially marked in cervical and submental regions. Low-grade fever present but not sufficient to keep patient confined to bed. Blood count made about December 20, 1923, revealed 27,000 leucocytes, but no differential count was made. Two days later complete count was made, revealing no decrease in red cells but marked changes in the whites, which numbered 19,000 cells, 20½ per cent polynuclear cells with 78½ per cent mononuclear cells, 70 per cent of which consisted of the large mononuclear variety consisting of many lymphoblasts and Reider forms. Counts were repeated at three- and four-day intervals, revealing on December 24, 14,300 cells with 22 per cent polynuclears and 78 per cent mononuclear cells; December 27, 16,000 cells with 14 per cent polynuclears and 86 per cent mononuclears. Another count made on December 31 gave 42 per cent polynuclear cells with 58 per cent mononuclears. Last count made some days later revealed almost normal relations of the various elements.

Fever continued for about two weeks with marked glandular swelling. This gradually subsided with a decrease in the cell count. Throat was extremely sore and revealed a firm whitish membrane over each tonsillar fossa, which was hard and dry to touch. It was difficult to remove any portion of membrane and smears failed to reveal spirochetes. Cultures revealed a pure culture of a streptococcus nonhemolytic in character, and showing a dirty brownish discoloration of blood agar.

Symptoms gradually subsided and patient returned slowly to normal. Entire time occupied by disease, about four weeks. Blood cultures were not made.

Blood Counts—All Kinds

Date	Reds	Whites	Polyms	Sm. L.	Monos. L.	Trans	Total Mononuclear
Dec. 20....		27,000					
Dec. 22....	4,960,000	19,000	20½	3	70½	5	79½
Dec. 24....		14,240	22	5	70	3	78
Dec. 27....		15,840	14	18	64	4	86
Dec. 31....		8,600	41½	7½	46	5	58½
Jan. 6.....		7,400	61	15	22	2	39

CASE No. 5. Mrs. R. W., age 24. Illness began on a Friday of September, 1924, with an apparent swelling on her face and lips. Patient says she thought it was lymph channels (having been a student of medicine). The same evening the swelling was quite marked. No evidence of enlargement of the glands. Next morning the swelling disappeared, but large areas of urticaria developed which cleared on taking a soda bath.

The second day the cervical glands began to enlarge and became about the size of walnuts. They were but slightly tender. The axillary and inguinal glands were also enlarged.

Patient's temperature gradually rose to 103 in the afternoon, coming up in a typical stepladder manner, lasted five days and subsided by lysis.

The third day the most distressing part of her complaint began, consisting of an extremely sore throat. A culture was made but found to contain no diphtheriae organisma, and a stained smear from slant revealed only cocci, type undetermined. Throat symptoms lasted for about two weeks.

The course of the disease was four weeks, and after a period of three months the patient feels perfectly well, although glands are still palpable.

Stools as described by patient were red with blood at times, but not confirmed by laboratory examinations.

Oxidase reaction proves cells to be of mononuclear and lymphoid origin.

COMMENT

Few blood diseases present such a striking picture. The early glandular enlargement, symptoms of discomfort in the mouth, and the blood picture presents the chief findings in cases of that dread and fatal disease, acute lymphatic leukemia as well. In fact, at times the course of the dis-

Date	Hbg.	Red Cells	White	Polys.	S. L.	L. L.	Eos.	Bas.	Tr.	Total Mono. Count
9/21/24	95%	5,470,000	18,100	16	75	4			5	84
9/22/24			18,200	18	66	7			9	82
9/24/24			13,500	18	76	4			2	82
9/27/24			7,550	33	56	6.5			4½	67
9/29/24			6,500	31	58	8	1		2	69
10/ 1/24			5,000	40.5	43.5	5	1	.5	4½	58
10/ 3/24			5,700	41	50	4	1	1	3	56
10/ 7/24		4,930,000	6,650	49	34.7	4	2	.3	8	49
10/12/24			4,100	47	44				9	53
10/19/24			3,700	28	61	6	2	1	2	69
10/28/24			6,250	36	50	6 Pol. M.		37½	5½	62
10/21/24			11,000	63	34					34

ease alone will give a final diagnosis and prove the benignancy of the condition.

Case No. 3 presented the most difficulties. This case was probably complicated by other conditions. Here we found the highest count on record in this disease, 48,000 per cu. mm. Pathologists and other consultants were of the opinion that acute lymphatic leukemia was the correct diagnosis. In spite of the predicted fatal termination the patient recovered and at the present time is normal in every way.

Many patients with this trouble remain undiagnosed on account of the moderate nature of the symptoms and the lack of careful study given to the laboratory findings. A simple leucocyte count will reveal an increase in cells, but the variety remains unknown, due to failure of a differential study. The period of leucocyte increase is not of long duration and the patient soon recovers, the symptoms being ascribed to any one of a number of common infections of the nose and throat.

DISCUSSION

NEWTON EVANS, M. D. (Loma Linda, California)—Doctor Butka has rendered a distinct service in calling attention to this interesting condition and, perhaps most important, in warning of the danger of confusing the condition with lymphatic leukemia. It is valuable to know that there is a condition which is so very similar to leukemia for which we must be on the lookout. As I see it, the most helpful, practical criterion in the differential diagnosis is the fact that, as a rule, the total leucocyte count in the infectious mononucleosis is not over 35,000. One of Doctor Butka's cases had a maximum leucocyte count of 48,000. It is an important question whether, as he suggests, this may have been due to some associated condition and was not an essential characteristic of the disease itself. If counts running up to 50,000 may be expected in infectious mononucleosis this fact will in itself make discrimination from lymphatic leukemia the more difficult.

This symptom complex, which is obviously an infectious process, presents another of that group of infectious diseases which are still unsolved problems as to etiology. Its comparative rarity makes it the more difficult for bacteriological study. It is to be hoped that some worker will be so fortunate as to have the opportunity and the ability to solve this problem. Its apparent slight tendency to produce any mortality would make it seem inconsequential, but the fact that it produces a definite period of morbidity with a prolonged convalescence, constitutes it as a disease of decided importance.

A. M. MOODY, M. D. (Saint Francis Hospital, San Francisco)—Doctor Butka's article is of considerable interest, as anyone directing laboratory work must from time to time come in contact with blood counts such as are here recorded. It has been my good fortune to observe a small number of these cases and to be able to differentiate them from lymphatic leukemia, which is important from the standpoint of prognosis.

The important laboratory point in differentiation is the presence in blood smears of many irregularly staining, degenerating and smudged types of mononuclear cells, together with a very high percentage of lymphocytes. Such blood pictures do not occur frequently, which, perhaps, can be illustrated by the fact that in over 4500 differential blood counts made in the Saint Francis Hospital laboratory since June 1, there is but one occurrance of this condition. This patient was from outside the hospital and one count only was taken.

The question of whether the disease should be called "infectious mononcleosis" or "acute glandular fever" seems to me to be unimportant. However, the term "acute glandular fever" is in keeping with the anatomical lesions present, whereas the mononucleosis undoubtedly is the result of, and therefore incidental to, the acute involvement of the lymph glands in this condition.

GERTRUDE MOORE, M. D. (Western Laboratories, Oakland, California)—In spite of its infrequency, infectious mononucleosis must always be borne in mind whenever one is tempted to make a diagnosis of acute lymphatic leukemia at the beginning of an illness which has as its outstanding symptoms fever, enlarged lymph glands, and a high absolute and relative mononuclear count. In order to avoid the error of a hopeless prognosis in these cases, we must watch developments and make repeated blood examinations until thoroughly typical blood changes have been demonstrated, for the blood changes in acute infectious mononucleosis are so similar to those of acute lymphatic leukemia as to deceive the most experienced hematologist at times. However, I believe the following points are helpful in the differentiation of these two conditions: First, the abnormal cells which are of the germinal center type of lymphoblasts have a wide variation in size, ranging from a cell distinctly smaller than the normal lymphocyte to one three or four times the size of a red blood cell; second, their protoplasm is hemogeneous and stains deeply in acute infectious mononucleosis, while in acute lymphatic leukemia both cytoplasm and nucleus show poor staining reaction; and, third, degenerated and fragile forms are frequent in leukemia but very infrequent in acute infectious mononucleosis. The final diagnosis can only be made when, in true leukemia, the blood count climbs to a point above 50,000, or, in acute infectious mononucleosis, drops gradually to normal with an accompanying subsidence of all symptoms.

DOCTOR BUTKA (closing)—The comparative rarity of this disease and the absence of an appreciable mortality contribute to the present day lack of knowledge regarding its true etiology. It is definitely infectious, but the nature of the offending organism is not known. Further investigation along this line will be made as opportunity arises.

During the recent session of Congress 17,800 bills were introduced—13,251 in the House, 4549 in the Senate—which breaks the record of the session two years ago, when 13,294 separate bills were proposed. Running debate on the floors of the two houses and speeches printed but not delivered used 13,000 pages of the "Congressional Record." Two years ago, at a comparable session, the Record ran a little under 12,000 pages.—Nation's Business.

The truth is that the thought of America is fashioned in great part by the republic's editors. Editors give counsel which makes for the republic's betterment; editors, in expressing their own views, tend to mold the views of their readers. Often they say coherently and forcefully what others of us have been thinking incoherently, and so give form to our thoughts and enable us the better to weigh them.—Hon. Thomas J. Lennon, Justice Supreme Court of California.